



Armed Forces College of Medicine AFCM





Diuretics (2)

By

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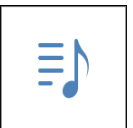


INTENDED LEARNING OBJECTIVES (ILO)

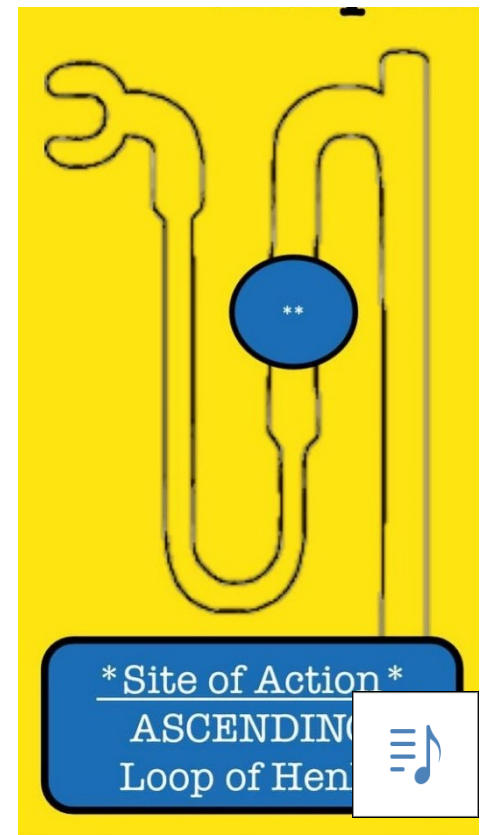


By the end of this lecture the student will be able to:

1. Identify different members of diuretics
2. Explain the mechanism of action of different diuretics
3. Relate the mechanism of action of diuretics to their clinical use
4. Explain the adverse effects of loop diuretics, thiazides.



Loop diuretics



LOOP DIURETICS

“Preparations”

**“Variable
Bioavailability”**

- **Frusemide**

- **Bumetanide**

- **Torsemide**

**“Most
Potent”**

Oral Dose = IV Dose

- **Ethacrynic acid**

**No Sulfonamides
hypersensitivity**

**90% of loop diuretics are bound to plasma
protein “albumin”**



LOOP DIURETICS

1. Most effective diuretics

- High Ceiling effect "Excretion of 20% of filtered Na^+ "
 - Release renal RBF & $\uparrow$ GFR $\uparrow$ $\downarrow$ Na^+ reabsorption
 - $\downarrow$ Medullary Hypertonicity Potent dehydrating effect
- Diuretics
Diuretics
Diuretics

Emergency

Hypertensive encephalopathy

Acute Pulmonary Edema
Venodilation

Refractory Edema to other Diuretics

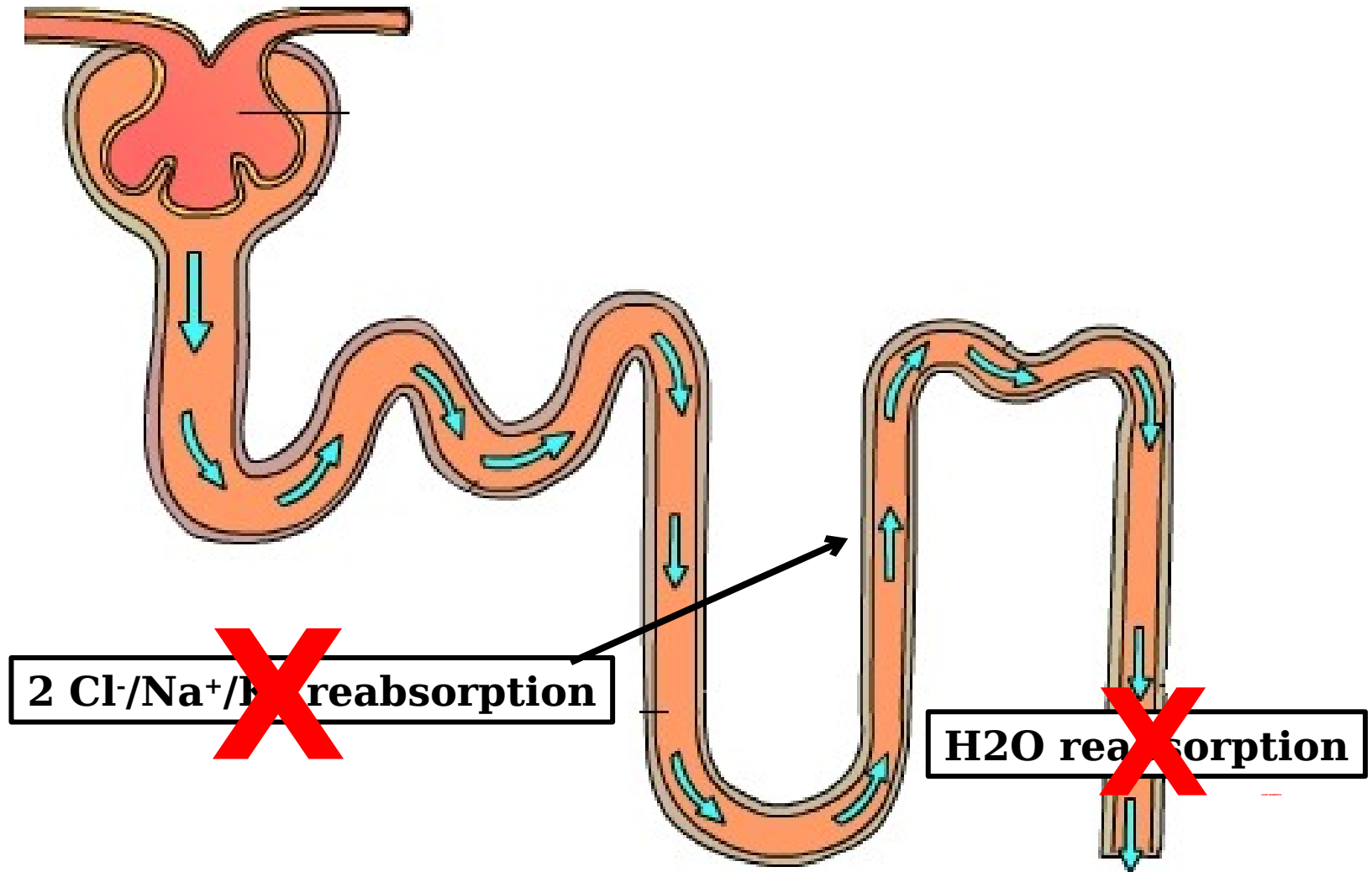
1. Liver cirrhosis & Nephrotic syndrome
2. Severe CHF
3. Renal impairment and Acute renal failure

+ Albumin

$\uparrow$ Dose to 5 folds.

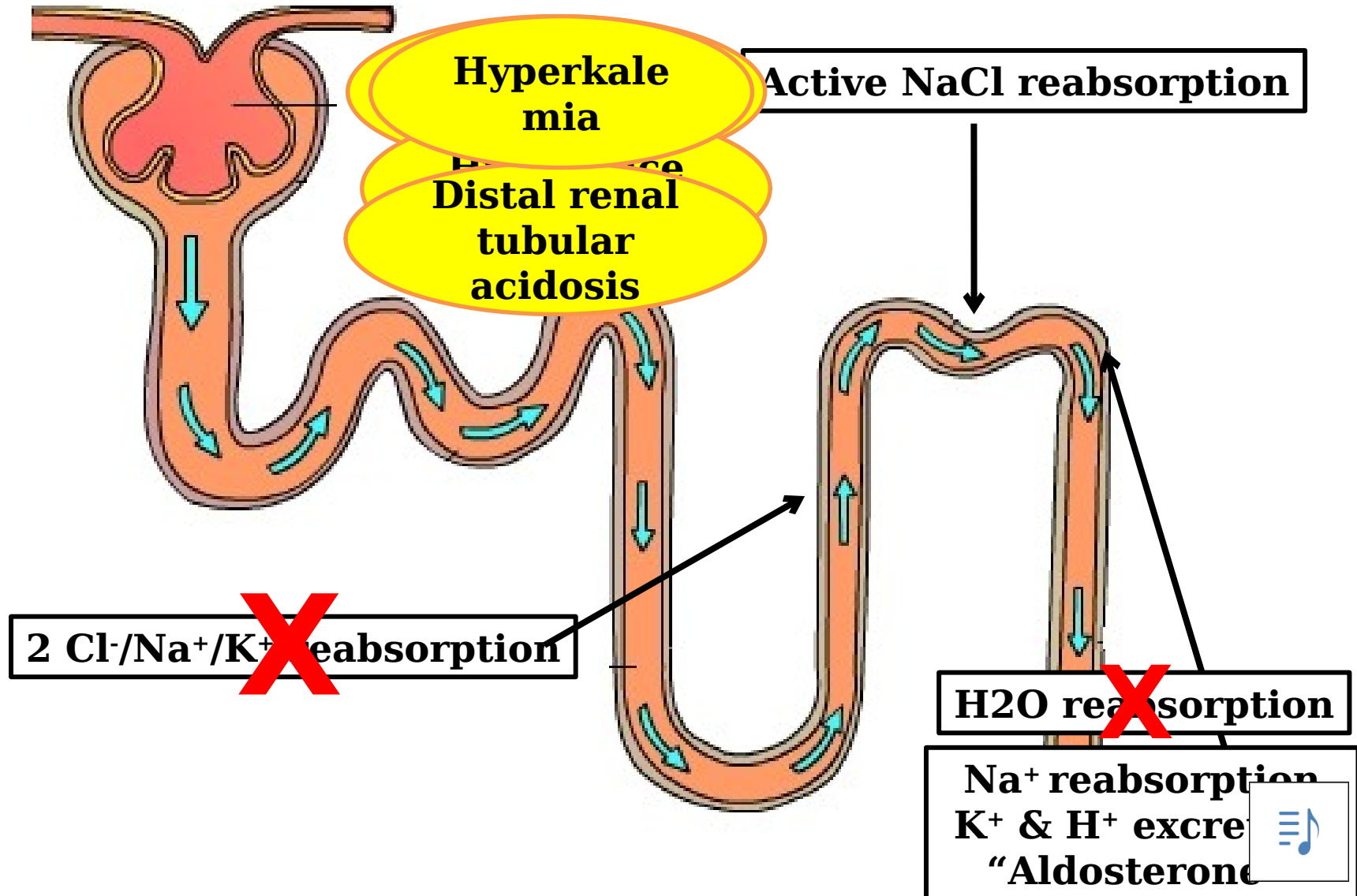


LOOP DIURETICS



LOOP DIURETICS

Other indications



LOOP DIURETICS

Adverse effects:

Hypokale
mia

Metabolic
alkalosis

Hypovolemia
and
Hemoconcentra
tion

Hypomagnese
mia

Hypocalcem
ia

Hyperuricemi
a

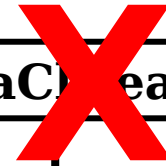


LOOP DIURETICS

Drug Interactions

1. THIAZIDE DIURETICS

Active NaCl reabsorption



LOOP DIURETICS

Block 2 $\text{Cl}^-/\text{Na}^+/\text{K}^+$ reabsorption

2. K-RETAINING
DIURETICS

Na^+ reabsorption
 K^+ & H^+ excretion
"Aldosterone"



LOOP DIURETICS

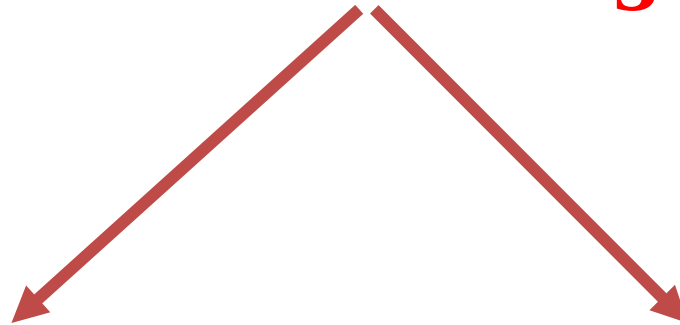
Other Drug Interactions

1. NS $\downarrow$ PG synthesis and $\downarrow$ action of loop diuretic
2. Aminoglycosid Ototoxicity
3. Cephalosporin Interstitial nephritis
4. Statin Myalgia (Bumetanide)





Causes of refractoriness to loop diuretics & its management



Pharmacokinetic
causes

Pharmacodynamic
causes



Pharmacokinetic causes

I. Defective intestinal absorption in decompensated HF

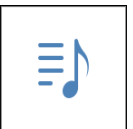
.Treatment: Give the diuretic IV

II. Defective pp binding in hypoalbuminemic states (liver cirrhosis & nephrotic syndrome) → extravascular diffusion of
:diuretic → ↓ renal excretion

.Treatment: Mix the diuretic with albumin prior to infusion

**III. Defective excretion of diuretics by acid secretory system in renal impairment due to accumulation of
:acids**

.Treatment: ↑ Dose of frusemide to 5 folds



Pharmacodynamic causes

I. Hypertrophy of distal tubular cells (on chronic use $\rightarrow$ $\uparrow$ Na^+ reabsorption $\rightarrow$ blunts the action of the diuretic):

Treatment: Add thiazides to inhibit Na^+ reabsorption in distal tubules & amplify the effect of loop diuretics.

II. Na^+ lost by loop diuretic is reabsorbed in exchange with K^+ in distal tubules (under the effect of aldosterone):



THIAZIDE DIURETICS

➤ **Moderately Powerful (Low Ceiling Effect)**

Hypertension

➤ **Vasodilator action**

**With
Chronic
Therapy**

↓ **GFR** → **Paradoxical Effect**
↓ **Urine volume**

↑ **Ca**

Patients on thiazides have a reduced risk of osteoporosis and hip fractures, thiazides are preferred in elderly hypertensive

tion

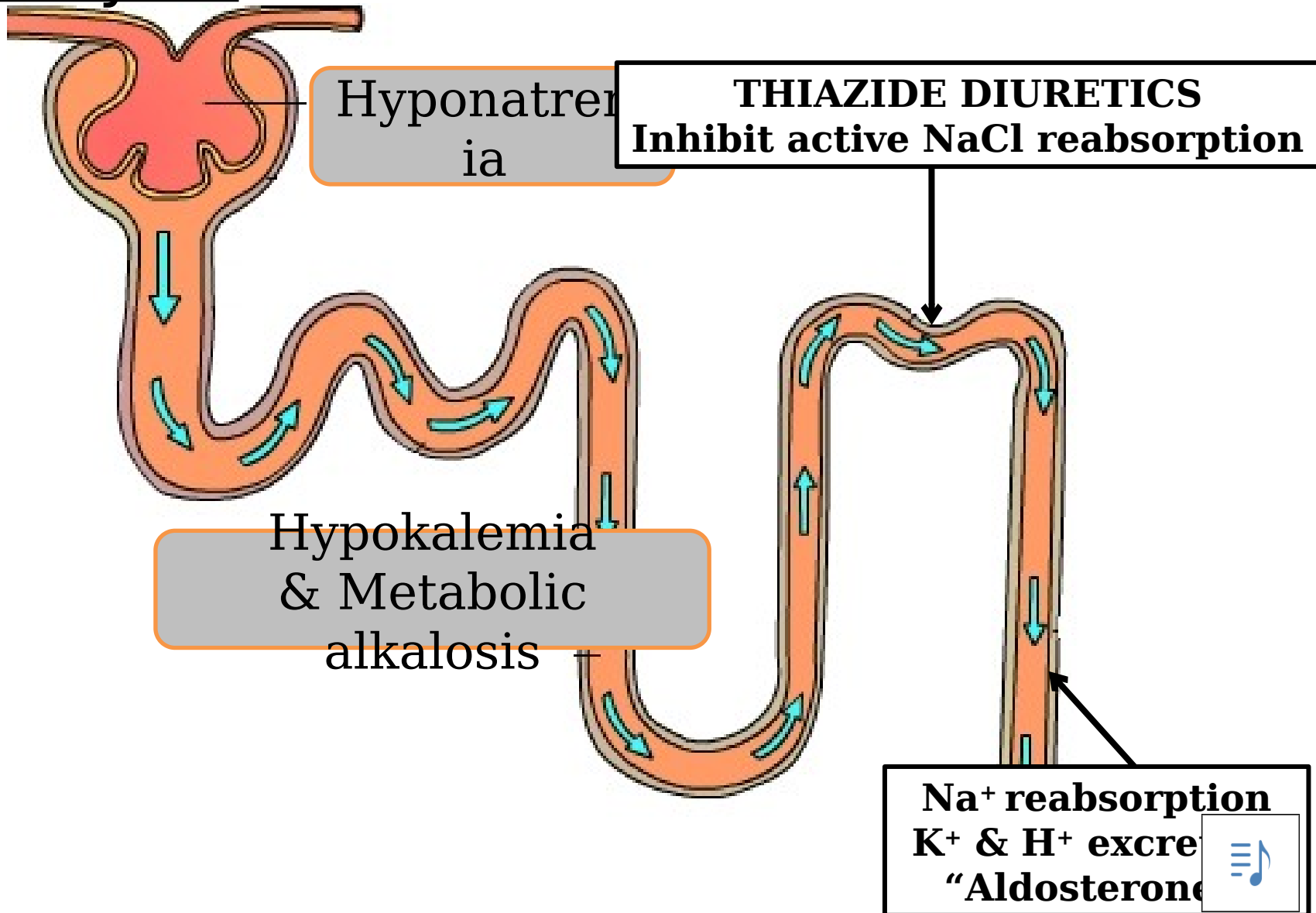
**Nephrogenic
diabetes insipidus**

**Idiopathic
hypercalciuria & Ca²⁺
stones**



THIAZIDE DIURETICS

Electrolytes



THIAZIDE DIURETICS

Precautions during use of Thiazide

➤ **Impaired renal function**

➤ **Liver cirrhosis**

➤ **DM**

➤ **Hyperlipidemia**

➤ **In male**

➤ **Gout**

ne

Hepatic

Glucose Encephalopathy

intolerance

↑ LDL &
↓ HDL

Impotence

Hyperuricemi
a



THIAZIDE DIURETICS “Preparations”

- Hydrochlorothiazide Short Acting

long acting

once/day

- Chlorthalidone

Most Potent & less metabolic
side effects

- Indapamide

- Metolazone

Effective in impaired renal
function



THIAZIDE DIURETICS

Drug Interactions

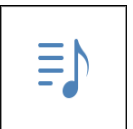
1. Loop Diuretics
2. K-sparing diuretics
3. Drugs cause hypokalemia
(β_2 agonist, insulin in large dose, loop diuretics)



Lecture quiz

An elderly patient with a history of heart disease is brought to the emergency room with difficulty breathing. Examination reveals that she has pulmonary edema. Which treatment is indicated?

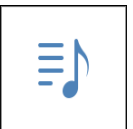
- A. Acetazolamide.
- B. Chlorthalidone.
- C. Furosemide.
- D. Hydrochlorothiazide.
- E. Spironolactone



Lecture quiz

A 55-year-old male with kidney stones has been placed on a diuretic to decrease calcium excretion. However, after a few weeks, he develops an attack of gout. Which diuretic was he taking?

- A. Furosemide.
- B. Hydrochlorothiazide.
- C. Spironolactone.
- D. Triamterene.
- E. Urea.



SUGGESTED TEXTBOOKS



1. Whalen, K., Finkel, R., & Panavelil, T. A. (2018) Lippincott's Illustrated Reviews: Pharmacology (7th edition.). Philadelphia: Wolters Kluwer
2. Katzung BG, Trevor AJ. (2018). Basic & Clinical Pharmacology (14th edition) New York: McGraw-Hill Medical.





Thank You